

X15642.NatlPhase.ST25.txt  
SEQUENCE LISTING

<110> Richard Dennis DiMarchi  
David Lee Smiley  
Lianshan Zhang

<120> MODIFIED GLUCAGON-LIKE PEPTIDE-1 ANALOGS

<130> X-15642 National Phase

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<170> PatentIn version 3.2

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Gln Ala Xaa Lys Xaa Phe Ile Xaa Trp Leu Xaa Xaa Gly Xaa Xaa Xaa
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<223> Xaa = Ser, His, Ser-NH<sub>2</sub>, His-NH<sub>2</sub>, L-Cys, D-Cys, homocysteine, penicillamine, NH<sub>2</sub>, or is absent

<220>

<221> MISC\_FEATURE

<222> (45)..(45)

<223> Xaa = L-Cys, D-Cys, homocysteine, penicillamine, NH<sub>2</sub>, or is absent

<400> 7

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly  
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Pro Xaa  
20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
35 40 45

<210> 8

<211> 31

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MISC\_FEATURE

<222> (1)..(1)

<223> Xaa = L-histidine, D-histidine, desamino-histidine, 2-amino-histidine beta-hydroxy-

histidine, homohistidine, alpha-fluoromethyl-histidine, or alpha-methyl-histidine

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<222> (2)..(2)

<223> Xaa = Ala, Gly, Val, Leu, Ile, Ser, or Thr

<220>

<221> MISC\_FEATURE

<222> (6)..(6)

<223> Xaa = Phe, Trp, or Tyr

<220>

<221> MISC\_FEATURE

<222> (10)..(10)

<223> Xaa = Val, Trp, Ile, Leu, Phe, or Tyr

<220>

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<222> (12)..(12)

<223> Xaa = Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val

<220>

<221> MISC\_FEATURE

<222> (13)..(13)

<223> Xaa = Tyr, Trp, or Phe

<220>

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<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa = Leu, Phe, Tyr, or Trp

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Xaa = Gly, Glu, Asp, Lys

<220>
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<223> Xaa = Ala, Val, Ile, or Leu

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<222> (21)..(21)
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<221> MISC_FEATURE
<222> (24)..(24)
<223> Xaa = Ala or Glu

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa = Val or Ile

<400> 8

Xaa Xaa Glu Gly Thr Xaa Thr Ser Asp Xaa Ser Xaa Xaa Glu Xaa
1      5      10      15

Gln Ala Xaa Lys Xaa Phe Ile Xaa Trp Leu Xaa Lys Gly Arg Lys
      20      25      30

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<211> 31
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<213> Artificial

<220>
<223> Synthetic construct

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2-amino-histidine, beta-hydroxy-
histidine, homohistidine, alpha-fluoromethyl-histidine, or
alpha-methyl-histidine

<220>
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<222> (2)..(2)
<223> Xaa = Gly, Ala, Val, Leu, Ile, Ser, or Thr

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<222> (10)..(10)
<223> Xaa = Val, Phe, Tyr, or Trp

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<223> Xaa = Ser, Tyr, Trp, Phe, Lys, Ile, Leu, or Val

<220>
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<222> (16)..(16)
<223> Xaa = Gly, Glu, Asp, or Lys

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<222> (19)..(19)
<223> Xaa = Ala, Val, Ile, or Leu

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<222> (27)..(27)
<223> Xaa = Val or Ile

<400> 9
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Xaa Ser Xaa Tyr Leu Glu Xaa
1 5 10 15

Gln Ala Xaa Lys Glu Phe Ile Ala Trp Leu Xaa Lys Gly Arg Lys
20 25 30

<210> 10
<211> 42
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<220>
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<222> (1)..(1)
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alpha-methyl-histidine

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<223> Xaa = Ala, Gly, Val, Leu, Ile, Ser, or Thr

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<222> (6)..(6)
<223> Xaa = Phe, Trp, or Tyr

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<222> (10)..(10)
<223> Xaa = Val, Trp, Ile, Leu, Phe, or Tyr

<220>
<221> MISC_FEATURE
<222> (12)..(12)
<223> Xaa = Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val

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<223> Xaa = Tyr, Trp, or Phe

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<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa = Leu, Phe, Tyr, or Trp

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<223> Xaa = Ala or Glu

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<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa = Val or Ile

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<221> MISC_FEATURE
<222> (28)..(28)
<223> Xaa = Lys, Asp, Arg, or Glu

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<222> (30)..(30)
<223> Xaa = Gly, Pro, or Arg

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<221> MISC_FEATURE
<222> (31)..(31)
<223> Xaa = Gly, Pro, Ser, or Lys

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<222> (32)..(32)
<223> Xaa = Ser, Pro, His, Lys, NH2

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<222> (33)..(33)
<223> Xaa = Ser, Arg, Thr, Trp, Lys, NH2 or is absent

<220>
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<222> (34)..(34)
<223> Xaa = Ser, Gly, Lys, NH2 or is absent

<220>

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<223> Xaa = Ala, Asp, Arg, Glu, Lys, Gly, NH2 or is absent

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<222> (36)..(36)
<223> Xaa = Pro, Ala, Lys, NH2 or is absent

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<222> (37)..(37)
<223> Xaa = Pro, Ala, Lys, NH2 or is absent

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<222> (38)..(38)
<223> Xaa = Pro, Ala, Arg, Lys, His, NH2 or is absent

<220>
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<222> (39)..(39)
<223> Xaa = Ser, His, Pro, Lys, Arg, NH2 or is absent

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<222> (40)..(40)
<223> Xaa = His, Ser, Arg, Lys, NH2, or is absent

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<221> MISC_FEATURE
<222> (41)..(41)
<223> Xaa = His, Ser, Arg, Lys, NH2, or is absent

<220>
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<222> (42)..(42)
<223> Xaa = Lys, NH2, or is absent

<400> 10
Xaa Xaa Glu Gly Thr Xaa Thr Ser Asp Xaa Ser Xaa Xaa Glu Xaa
1      5      10      15

Gln Ala Xaa Lys Xaa Phe Ile Xaa Trp Leu Xaa Xaa Gly Xaa Xaa Xaa
20      25      30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
35      40

<210> 11
<211> 42
<212> PRT
<213> Artificial

<220>
<223> Synthetic construct

<220>
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<222> (1)..(1)
<223> Xaa = L-histidine, D-histidine, desamino-histidine,
2-amino-histidine, beta-hydroxy-
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histidine, homohistidine, alpha-fluoromethyl-histidine, or  
alpha-methyl-histidine

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<220>
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<222> (2)..(2)
<223> Xaa = Gly, Val, Leu, Ile, Ser, or Thr

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa = Val, Trp, Ile, Leu, Phe, or Tyr

<220>
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<222> (16)..(16)
<223> Xaa = Gly, Glu, Asp, or Lys

<220>
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<222> (19)..(19)
<223> Xaa = Ala, Val, Ile, or Leu

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa = Val or Ile

<220>
<221> MISC_FEATURE
<222> (28)..(28)
<223> Xaa = Lys, Asp, Arg, or Glu

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<222> (30)..(30)
<223> Xaa = Gly, Pro, or Arg

<220>
<221> MISC_FEATURE
<222> (31)..(31)
<223> Xaa = Gly, Pro, Ser or Lys

<220>
<221> MISC_FEATURE
<222> (32)..(32)
<223> Xaa = Ser, Pro, His, Lys, NH2 or is absent

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<223> Xaa = Ser, Arg, Thr, Trp, Lys, NH2 or is absent

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<223> Xaa = Ser, Gly, Lys, NH2 or is absent

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<222> (35)..(35)
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<220>
<221> MISC_FEATURE
<222> (36)..(36)

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<223> Xaa = Pro, Ala, Lys, NH2 or is absent

<220>
<221> MISC_FEATURE
<222> (37)..(37)
<223> Xaa = Pro, Ala, Lys, NH2, or is absent

<220>
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<222> (38)..(38)
<223> Xaa = Pro, Ala, Arg, Lys, His, NH2 or is absent

<220>
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<222> (39)..(39)
<223> Xaa = Ser, His, Pro, Lys, Arg, NH2 or is absent

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<222> (40)..(40)
<223> Xaa = His, Ser, Arg, Lys, NH2 or is absent

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<222> (41)..(41)
<223> Xaa = His, Ser, Arg, Lys, NH2 or is absent

<220>
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<222> (42)..(42)
<223> Xaa = Lys, NH2, or is absent

<400> 11
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Xaa Ser Ser Tyr Lys Glu Xaa
1 5 10 15
Gln Ala Xaa Lys Glu Phe Ile Ala Trp Leu Xaa Xaa Gly Xaa Xaa Xaa
20 25 30
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
35 40

<210> 12
<211> 42
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<220>
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<222> (1)..(1)
<223> Xaa = L-histidine, D-histidine, desamino-histidine,
2-amino-histidine, beta-hydroxy-histidine, homohistidine,
alpha-fluoromethyl-histidine, or alpha-methyl-histidine

<220>
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<222> (2)..(2)
<223> Xaa = Gly, Val, Leu, Ile, Ser, or Thr

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<222> (16)..(16)
<223> Xaa = Gly, Glu, Asp, or Lys

<220>
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<222> (19)..(19)
<223> Xaa = Ala, Val, Ile, or Leu

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa =Val or Ile

<220>
<221> MISC_FEATURE
<222> (32)..(32)
<223> Xaa= Ser, Pro, His, Lys, NH2 or is absent

<220>
<221> MISC_FEATURE
<222> (33)..(33)
<223> Xaa = Ser, Arg, Thr, Trp, Lys, NH2 or is absent

<220>
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<222> (34)..(34)
<223> Xaa = Ser, Gly, Lys, NH2 or is absent

<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> Xaa = Ala, Asp, Arg, Glu, Lys, Gly, NH2 or is absent

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Xaa = Pro, Ala, Lys, NH2 or is absent

<220>
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<222> (37)..(37)
<223> Xaa = Pro, Ala, Lys, NH2 or is absent

<220>
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<222> (38)..(38)
<223> Xaa = Pro, Ala, Arg, Lys, His, NH2 or is absent

<220>
<221> MISC_FEATURE
<222> (39)..(39)
<223> Xaa = Ser, His, Pro, Lys, Arg, NH2 or is absent

<220>
<221> MISC_FEATURE
<222> (40)..(40)
<223> Xaa = His, Ser, Arg, Lys, NH2, or is absent

<220>
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<222> (41)..(41)
<223> Xaa = His, Ser, Arg, Lys, NH2 or is absent

<220>
<221> MISC_FEATURE

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&lt;222&gt; (42)..(42)

&lt;223&gt; Xaa = Lys, NH2, or is absent

&lt;400&gt; 12

Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Lys Glu Xaa  
 1 5 10 15

Gln Ala Xaa Lys Glu Phe Ile Ala Trp Leu Xaa Lys Gly Gly Pro Xaa  
 20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
 35 40

&lt;210&gt; 13

&lt;211&gt; 45

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Synthetic construct

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (1)..(1)

<223> Xaa = L-histidine, D-histidine, desamino-histidine,  
 2-amino-histidine, beta-hydroxy-histidine, homohistidine,  
 alpha-fluoromethyl-histidine, or alpha-methyl-histidine

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (2)..(2)

&lt;223&gt; Xaa = Ala, Gly, Val, Leu, Ile, Ser, or Thr

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (6)..(6)

&lt;223&gt; Xaa = Phe, Trp or Tyr

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (10)..(10)

&lt;223&gt; Xaa = Val, Trp, Ile, Leu, Phe, or Tyr

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (12)..(12)

&lt;223&gt; Xaa = Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (13)..(13)

&lt;223&gt; Xaa = Tyr, Trp, or Phe

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (14)..(14)

&lt;223&gt; Xaa = Leu, Phe, Tyr, or Trp

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (16)..(16)

&lt;223&gt; Xaa = Gly, Glu, Asp, or Lys

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<223> Xaa = Gly, Pro, or Ser

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<220>
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<222> (44)..(44)
<223> Xaa = Ser, His, Lys, NH2 or is absent

<220>
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<222> (45)..(45)
<223> Xaa = Lys, NH2 or is absent

<400> 13

Xaa Xaa Glu Gly Thr Xaa Thr Ser Asp Xaa Ser Xaa Xaa Xaa Glu Xaa
1          5          10          15

Gln Ala Xaa Lys Xaa Phe Ile Xaa Trp Leu Xaa Xaa Gly Xaa Xaa Xaa
          20          25          30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
          35          40          45

<210> 14
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<222> (32)..(32)
<223> Xaa = Ser, Pro, or His

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<223> Xaa = Ser, Arg, Thr, Trp, or Lys

<220>
<221> MISC_FEATURE
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<223> Xaa = Ser, or Gly

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<223> Xaa = Pro, Ala, Lys, NH2 or is absent

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<222> (38)..(38)
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<222> (45)..(45)
<223> Xaa = Lys, NH2 or is absent

<400> 14

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His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly  
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Pro Xaa  
 20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
 35 40 45

<210> 15

<211> 31

<212> PRT

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<220>

<223> Synthetic construct

<220>

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<222> (1)..(1)

<223> Xaa = L-histidine, D-histidine, desamino-histidine,  
 2-amino-histidine, beta-hydroxy-

histidine, homohistidine, alpha-fluoromethyl-histidine, or  
 alpha-methyl-histidine

<220>

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<222> (2)..(2)

<223> Xaa = Ala, Gly, Val, Leu, Ile, Ser or Thr

<220>

<221> MISC\_FEATURE

<222> (6)..(6)

<223> Xaa = Phe, Trp, Tyr

<220>

<221> MISC\_FEATURE

<222> (10)..(10)

<223> Xaa = Val, Trp, Ile, Leu, Phe, or Tyr

<220>

<221> MISC\_FEATURE

<222> (12)..(12)

<223> Xaa = Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val

<220>

<221> MISC\_FEATURE

<222> (13)..(13)

<223> Xaa = Tyr, Trp, or Phe

<220>

<221> MISC\_FEATURE

<222> (14)..(14)

<223> Xaa = Leu, Phe, Tyr, or Trp

<220>

<221> MISC\_FEATURE

<222> (16)..(16)

<223> Xaa = Gly, Glu, Asp, Lys

<220>

<221> MISC\_FEATURE

&lt;222&gt; (19)..(19)

&lt;223&gt; Xaa = Ala, Val, Ile, or Leu

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (21)..(21)

&lt;223&gt; Xaa = Glu, Ile, or Ala

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (24)..(24)

&lt;223&gt; Xaa = Ala or Glu

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (27)..(27)

&lt;223&gt; Xaa = Val or Ile

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (31)..(31)

&lt;223&gt; Xaa = Gly, His, Lys, or NH2 or is absent

&lt;400&gt; 15

Xaa Xaa Glu Gly Thr Xaa Thr Ser Asp Xaa Ser Xaa Xaa Xaa Glu Xaa  
 1 5 10 15

Gln Ala Xaa Lys Xaa Phe Ile Xaa Trp Leu Xaa Lys Gly Arg Xaa  
 20 25 30

&lt;210&gt; 16

&lt;211&gt; 31

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Synthetic construct

&lt;400&gt; 16

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly  
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly  
 20 25 30

&lt;210&gt; 17

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Synthetic construct

&lt;400&gt; 17

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Glu  
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Ile Lys Gly Gly Pro Ser  
 20 25 30

Ser Gly Ala Pro Pro Pro Cys  
35

<210> 18  
<211> 39  
<212> PRT  
<213> Artificial

<220>  
<223> Synthetic construct

<220>  
<221> MOD\_RES  
<222> (39)..(39)  
<223> 2,2'-dithiolbis(5-dinitropyridine) is attached to the thiol of  
Cys at position 39

<400> 18

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Glu  
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Ile Lys Gly Gly Pro Ser  
20 25 30

Ser Gly Ala Pro Pro Pro Cys  
35

<210> 19  
<211> 32  
<212> PRT  
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<220>  
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<400> 19

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Glu  
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Ile Lys Gly Arg Gly Cys  
20 25 30

<210> 20  
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<212> PRT  
<213> Artificial

<220>  
<223> Synthetic construct

<220>  
<221> MOD\_RES  
<222> (32)..(32)  
<223> S-sulfonate (SS03) is attached to the thiol of Cys at position 32

&lt;400&gt; 20

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Glu  
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Ile Lys Gly Arg Gly Cys  
 20 25 30

&lt;210&gt; 21

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Synthetic construct

&lt;400&gt; 21

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Glu  
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Ile Lys Gly Arg Gly Lys  
 20 25 30

&lt;210&gt; 22

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Synthetic construct

&lt;220&gt;

&lt;221&gt; MOD\_RES

&lt;222&gt; (32)..(32)

&lt;223&gt; [3-(2-pyridyl)dithio]propanamide]amide is attached to Lys at position 32

&lt;400&gt; 22

His Val Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Glu  
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Ile Lys Gly Arg Gly Lys  
 20 25 30

&lt;210&gt; 23

&lt;211&gt; 39

&lt;212&gt; PRT

&lt;213&gt; Heloderma suspectum

&lt;220&gt;

&lt;221&gt; MISC\_FEATURE

&lt;222&gt; (1)...(39)

&lt;223&gt; Exendin-3

&lt;400&gt; 23

His Ser Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu  
 Page 29

1 5 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser  
20 25 30

Ser Gly Ala Pro Pro Pro Ser  
35

<210> 24  
<211> 39  
<212> PRT  
<213> Heloderma suspectum

<220>  
<221> MISC\_FEATURE  
<222> (1)..(39)  
<223> Exendin-4

<400> 24

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu  
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser  
20 25 30

Ser Gly Ala Pro Pro Pro Ser  
35